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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,844	03/04/2004	Peter G. Zaphiropoulos	2921-0145P	5375

2292 7590 08/17/2006

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 08/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,844	ZAPHIROPOULOS ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *6-12 and 14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/807,007.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibit A*.

DETAILED ACTION

RE: Zaphiropoulos et al.

1. Applicant's election of Group I (claims 1-5 and 13) drawn in part to an isolated human protein, which is essentially comprised of SEQ ID NO.1, and a medicament comprising a protein according to claims 1-4 in the reply filed on 6/26/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The information disclosure statement (IDS) filed on 3/4/04 has been considered. A signed copy is attached hereto.

3. Claims 1-18 are pending. Claims 6-12 and 14-18 are withdrawn from further consideration as being drawn to non-elected inventions.

4. Claims 1-5 and 13 are under examination.

Specification

5. The amendment to the specification filed on 3/4/04 is objected to because of the following informalities: The page number mentioned on page 3 of the amendment appears to be incorrect. On page 3, line 12, the phrase "page 5, line 28" should be "page 6, line 28". On page 3, line 13, the phrase "page 6, line 3" should be "page 7, line 3".

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-5 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-5 and 13 are indefinite for reciting "capable of participating in the human PTCH/SHH pathway" in claims 1-4 because the phrase is not clear. Does the protein participate in the pathway or not and what does "participating" encompass? Does participating mean directly binds the SHH or does the protein interact with another protein that has some involvement with the SHH protein or PTCH proteins?

b. Claims 1, 5 and 13 are indefinite for reciting the phrase "essentially comprised of SEQ ID NO.1" in claim 1. The meaning of the phrase is not clear. Does it mean the protein comprises SEQ ID NO.1 or comprises sequences that are essentially similar to SEQ ID NO.1?

Claim Rejections - 35 USC § 101 and - 35 USC § 112,1nd paragraph

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5 and 13 are rejected under 35 U.S.C.101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to an isolated human protein capable of participating in the human PTCH/SHH pathway during embryonic development and/or carcinogenesis, which is essentially comprised of SEQ ID NO.1, which comprises at least about 1000, 1040, or 1100 amino acids as listed in SEQ ID NO.1, a medicament comprising such protein and a kit comprising such protein.

The instant specification discloses that the protein of SEQ ID NO.1, i.e. PTCH2 is 57% identical to PTCH1, with a significantly variable region present between the transmembrane domains 6 and 7, and 91% identical to the mouse PTCH2 sequence (see page 20, lines 26-29). The specification teaches PTCH2 protein exhibits substantial differences in sequence and functions when compared to human PTCH1 protein (see page 11, lines 16-18). The specification teaches that the function of PTCH2 is similar to human PTCH1 but distinct in certain ways (see page 11, lines 18-21). The specification teaches that the mouse and zebrasigh homologs of PTCH2 have been reported to be expressed in partly overlapping pattern with PTCH1 during embryonic development and to be induced by SHH (see page 22, lines 25-27). The specification teaches that the extracellular loops in PTCH1 are presumed to be involved in binding of the ligand SHH (see specification page 21, lines 29-31). The specification teaches that in basal cell carcinoma (BCC) having frequent mutations in the PTCH1 gene, the

expression of the PTCH2 mRNAs in upregulated (see specification, page 23, lines 10-11). There is no other disclosure of any chemical, physical, or biological properties of the protein. The specification as filed does not disclose or provide any evidence that points to an activity for the protein and furthermore there is no art of record that discloses or suggests any activity for the claimed protein. Therefore, there is no well-established utility.

Based upon the fact that the protein of SEQ ID NO.1 shares homology with PTCH1 and mouse PTCH2, the specification states that the claimed protein can be used in the pharmaceutical industry, for example, it will provide information that eventually may enable cells from fetal tissue, which may be transplanted into patients suffering from e.g. Parkinson's disease or cancer, such as BCC (see page 18, lines 3-4). However the specification as filed does not disclose or provide any evidence that points to the function for the protein and protein fragments (i.e. a protein comprising at least 1000, 1040, or 1100 amino acids of SEQ ID NO.1). The specification does not disclose a correlation of the protein PTCH2 to any diseases because the specification has not shown that the expression of protein PTCH2 is indeed related to any diseases, such as cancer including BCC. Moreover, one of skill in the art cannot extrapolate the sequence homology data to the function of the PTCH2 protein, how the instantly claimed protein correlates to the human disease because the protein chemistry is unpredictable. It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding

Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2). Thus in the instant case, one of skill in the art would not be able to predict if an amino acid having 57% identity to PTCH1

has the same function as PTCH1. Moreover, there is no teaching in the prior art regarding the function and activity of the mouse PTCH2 protein, and a correlation of the mouse PTCH2 protein to any diseases.

This situation is extremely analogous to example 4 of the Utility Guidelines, where a protein was disclosed by reference to a SEQ ID number and methods of making the protein, but fails to disclose any chemical, physical, or biological properties for the protein other than the sequence, was found to lack utility. In the current case, the PTCH2 protein and fragment thereof lack any substantial utility whatsoever. The specification does not even show that how the protein is endogenously expressed in different tissues. So this case is similar to the uncharacterized protein of Example 4, since it lacks a substantial utility because there is no "real world" context of use. Further research would be required to identify and reasonably confirm a "real world" context of use PTCH2. As noted in the utility guidelines, basic research on a product to identify properties and intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials).

Since neither the specification nor the art of record discloses any diseases or conditions caused or exacerbated by protein PTCH2, the asserted utility in this case essentially is a method of diagnosing and treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of used. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of the use. Therefore, claims have no specific and substantial utility.

As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". The specification does not provide any evidence indicating a possible therapeutic use and simply represents a protein which may be expressed in a tissue. Until some function or some activity of the protein is identified, the protein has no use. Therefore, there is no specific utility for this protein until a specific biological function or activity is identified.

With regard to the utility analysis, the current situation directly tracks Examples 4 and 12 of the utility guidelines, where a protein of entirely unknown function and a receptor with an unknown ligand was characterized as lacking utility.

Given the teachings of unpredictability associated with protein chemistry and the lack of functional description in the specification, one of skill in the art cannot with any certainty correlate the teachings of the instant specification with any specific disease diagnosis and therapeutics. Because the specification has not taught how the instantly claimed protein functions, what its cellular role is, and what specific or substantial use the claimed polypeptide would have. As such, the specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide and fragments thereof. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

10. Claims 1-5 and 13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

11. Claims 1-5 and 13 are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to an isolated human protein capable of participating in the human PTCH/SHH pathway during embryonic development and/or carcinogenesis, which is essentially comprised of SEQ ID NO.1, which comprises at least about 1000, 1040, or 1100 amino acids as listed in SEQ ID NO.1, a medicament comprising such protein and a kit comprising such protein.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The isolated protein encompasses the amino acid which is essentially comprised of SEQ ID NO.1, or which comprises at least about 1000, 1040 or 1100 amino acids as listed in SEQ ID NO.1.

Quantity of experimentation

The quantity of experimentation is extremely large because the specification does not teach the function and activity for the claimed proteins (i.e. SEQ ID NO.1 and a protein comprising at least 1000, 1040, or 1100 amino acids of SEQ ID NO.1). Furthermore there is no art of record that discloses or suggests any activity for the claimed protein. The specification does not teach a correlation of the claimed proteins to any diseases. While the specification teaches that the protein of SEQ ID NO.1 shares homology to PTCH1, one cannot extrapolate the function of PTCH1 to that of PTCH2 based on the sequence homology because the protein chemistry is highly unpredictable. While the specification teaches that PTCH2 mRNA is overexpressed in BCC, the expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide. As such, it will require undue experimentation to characterize the protein and thereafter use the protein.

The state of the prior art and the predictability or lack thereof in the art:

Those of skill in the art, recognize that expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. Greenbaum et al. (Genome Biology, 2003, Vol. 4, Issue 9, pages 117.1-117.8) cautions against assuming that mRNA levels are generally correlative of protein levels. The reference teaches (page 117.3, 2nd column) that primarily because of a limited ability to measure protein abundances, researchers have tried to find correlations between mRNA and the limited protein expression data, in the hope that they could determine protein abundance levels from the more copious and technically easier mRNA experiments. To date, however, there have been only a handful of efforts to find correlations between mRNA and protein expression levels, most notably in human cancers and yeast cells. And, for the most part, they have reported only minimal and/or limited correlations. The reference further teaches (page 117.4, 2nd column) that there are presumably at least three reasons for the poor correlations generally reported in the literature between the level of mRNA and the level of protein, and these may not be mutually exclusive. First, there are many complicated and varied post-transcriptional mechanisms involved in turning mRNA into protein that are not yet sufficiently well defined to be able to compute protein concentrations from mRNA; second, proteins may differ substantially in their *in vivo* half lives; and/or third, there is a significant amount of error and noise in both protein and mRNA experiments that limit our ability to get a clear picture. The reference further notes (page 117.6, page 2nd column) that to be fully able to understand the relationship between mRNA and protein abundances, the dynamic

processes involved in protein synthesis and degradation have to be better understood. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) illustrate post-transcriptional regulation of ferritin wherein the translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Also, with regards to tumor associated antigens, Fu et al. (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Furthermore, Mallampalli et al. (Biochem. J. 1996, Vol. 318, pages 333-341) teach that the glucocorticoid, betamethasone, increased mRNA expression of cholinephosphate cytidylyltransferase (CT) as determined by RT-PCR and Southern analysis, but did not alter the levels of the CT enzyme as assayed by Western blotting (abstract, and page 339, 2nd column, 2nd paragraph). Thus, the predictability of protein translation and its possible utility as a diagnostic or therapeutic are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation.

Thus, in the absence of a correlation between the claimed proteins and any diseases, such as cancer, the information obtained from over expression of the mRNA of PTCH2 in BCC only serves as the basis for further research on the observation itself. Therefore, absent evidence of the protein's expression including a correlation to any

diseased state, one of skill in the art would not be able to predictably use the claimed proteins without undue experimentation.

Working examples:

The instant specification discloses that the protein of SEQ ID NO.1, i.e. PTCH2 is 57% identical to PTCH1, with a significantly variable region present between the transmembrane domains 6 and 7, and 91% identical to the mouse PTCH2 sequence (see page 20, lines 26-29). The specification teaches that in basal cell carcinoma (BCC) having frequent mutations in the PTCH1 gene, the expression of the PTCH2 mRNAs in upregulated (see specification, page 23, lines 10-11). Based upon the fact that the protein of SEQ ID NO.1 shares homology with PTCH1 and mouse PTCH2, and PTCH2 mRNA is expressed in BCC, the specification states that the claimed protein can be used in the pharmaceutical industry, for example, it will provide information that eventually may enable cells from fetal tissue, which may be transplanted into patients suffering from e.g. Parkinson's disease or cancer, such as BCC (see page 18, lines 3-4). However the specification as filed does not disclose or provide any evidence that points to the function for the protein and protein fragments (i.e. a protein comprising at least 1000, 1040, or 1100 amino acids of SEQ ID NO.1). Furthermore there is no art of record that discloses or suggests any activity for the claimed proteins. While the specification teaches mRNA of PTCH2 is overexpressed in BCC, it fails to show that the protein PTCH2 is also overexpressed in BCC. Without such information, one skilled in

the art would not know how to use the protein of SEQ ID NO.1, and fragments thereof (i.e. a protein comprising at least 1000, 1040, or 1100 amino acids of SEQ ID NO.1).

Guidance in the specification

It is art known that certain residues are shown to particularly important to the biological or structural properties of a protein or peptide, e.g., residues in active sites and such residues may not be generally be exchanged. Skolnick et al teach that sequence-based methods for function prediction are inadequate and knowing a protein's structure does not tell one its function (Skolnick, et al. Trends in Biotech. 18, 34-39, 2000, see abstract, in particular). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. The specification teaches that PTCH1 is involved in PTCH/SHH pathway and is mutated in BCC. However, the specification does not disclose that PTCH2 has same function as PTCH1. One cannot extrapolate the function of PTCH1 to that of PTCH2 based upon their sequence homology because the protein chemistry is unpredictable. Moreover, there is no indication in the disclosure that the protein PTCH2 is overexpressed in BCC. Without the guidance on the activity and function of PTCH2, it would require undue experimentation practice the instant inventions.

Level of skill in the art

The level of the skill in the art is deemed to be high

Conclusion:

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by de Sauvage et al. (US Patent No. 6,709,838B1, Date of Patent 3/23/2004, earliest effective filing date 4/15/1998).

Claims 1 and 5 are drawn to an isolated human protein capable of participating in the human PTCH/SHH pathway during embryonic development and/or carcinogenesis, which is essentially comprised of SEQ ID NO.1, and a medicament, comprising said protein. Due to the indefinite nature of the claims (see paragraph 7b above), the phrase" essentially comprised of" is interpreted here as "comprising sequences that are essentially similar to SEQ ID NO.1".

de Sauvage et al. teach an isolated patched-2 polypeptide of SEQ ID NO.2 (see column 2, lines 62-67) and a therapeutic formulation of the composition comprising the polypeptide of SEQ ID NO.2 and a pharmaceutically acceptable carrier (see column 32, lines 33-40). de Sauvage et al. teach that patched-2 of SEQ ID NO.2 can bind to all the members of the Hedgehog family (see column 18, lines 21-26). Hedgehog signaling pathway is implicated in the formation of embryonic structures in mammals and invertebrates (see column 18, lines 13-15). The SEQ ID NO.2 of de Sauvage et al. is 99.7% identical to the instant SEQ ID NO.1 (see sequence alignment Exhibit A). Because the indefinite nature of "essentially comprise of" (see paragraph 7b above), the patched-2 polypeptide of SEQ ID NO.2 of de Sauvage reads on the instant inventions.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, PhD
Art Unit 1643
Aug. 9, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER